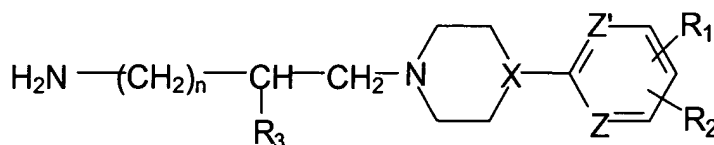


(VI)

with a compound having the structure of Formula V in pyridine at reflux temperature followed by reflux in the presence of acetic anhydride



(V)

thereby to produce the compound of Formula II.

### Remarks

Claims 44 and 45 have been amended to point out the invention. New claims 48 and 49 have been added. Support for the amendments and new claims is found in applicants' specification as filed. For example, support for separately claiming  $m=0$  (claim 44) and  $m=1-3$  (claim 48), and similarly  $m'=1$  (claim 45) and  $m'=2-4$  (claim 49) is found in the list of compounds from page 7, line 15 to page 8, line 20, illustrating both 2,6-dioxopiperidin-1-yl and 2,5-dioxopyrrolidin-1-yl groups. No new matter is introduced thereby.

Rejection Under 35 U.S.C. §102(b) over Wu et al. (J.Med.Chem., v.12, (1969), 876-881) and Khadilkar et al. (J.Ind.Chem.Soc., v.VLXII, (1986) 529-530)

Claims 44 and 45 have been rejected as anticipated by Wu et al. and Khadilkar et al. Applicants respectfully traverse the rejection for the following reasons.

As presented herein, the pending claims are not anticipated by either Wu et al. or Khadilkar. Wu et al. discloses certain 2,4-dioxo-3-azaspiro decanes and undecanes, as well as certain glutarimides, including methods of making such compounds. See Wu et al., general structure, p. 876, and structures in Table 1, p. 877. The general structure (Wu et al., p. 876) has broken lines indicating the variable carbon skeletons disclosed. Although glutarimides are disclosed as compounds 41-52 in Table 1 of Wu et al., no succinimides are disclosed. The substituents which are disclosed as being present in the phenyl ring portion of the glutarimides of Wu et al. are H and *o*-OCH<sub>3</sub>.

Khadilkar et al. discloses certain succinimides, and methods of making such compounds. See Khadilkar et al., structure of compound 4, p. 529, and compounds 4a-4g in Table 1, p. 530. The substituents which are disclosed as being present in the phenyl ring portion of the succinimides of Khadilkar et al. are H, 2-, 3-, and 4-CH<sub>3</sub>, and 2-, 3-, and 4-Cl.

The pending claims as amended claim processes for the preparation of compounds which are different from the compounds disclosed in either Wu et al. or Khadilkar et al. Claims 44 and 45 which cover particular succinimides, do not claim R<sub>1</sub> or R<sub>2</sub> as H, Cl, or CH<sub>3</sub>. Claims 48 and 49, which cover particular glutarimides, do not claim R<sub>1</sub> or R<sub>2</sub> as H or OCH<sub>3</sub>. Since the compounds of the present invention are novel and not anticipated by the prior art of record, the processes to prepare the novel compounds are also not anticipated. Applicants respectfully request reconsideration and withdrawal of the rejections.

Rejection Under 35 U.S.C. § 103 over Wu et al., New et al. (United States Patent No. 4,524,206) and Khadilkar et al.

Claims 44 and 45 have been rejected as obvious over Wu et al., New et al., and Khadilkar et al. Applicants respectfully traverse the rejection for the following reasons.

As is well known, to establish a prima facie case of obviousness, three criteria must be met. First, there must be motivation in the prior art to modify the reference. Second, there must be a reasonable expectation of success, and third, the prior art reference must teach or suggest all the claimed limitations. In this connection, all the teachings and suggestions, and expectation of success must come from the prior art, and not from applicants' disclosure.

There is no suggestion in Wu et al., New et al., or Khadilkar et al. of the desirability of modifying the reactions disclosed in these references to obtain the novel compounds for the high

$\alpha_1$ -AR selectivity for use in BPH disclosed in the present invention. Further, it is clear that neither problem nor solution is discernible to one with ordinary skill in the art from the teachings of prior art references.

The arguments presented above with respect to the cited prior art have been presented previously in this case (See applicants' "Amendment and Response to Office Action" mailed January 2, 2002). In response to these arguments, the Examiner indicated that "[a]pplicants arguments regarding the rejections under 35 U.S.C. 102, 103 and 112 in the office action in paper number 4, sent 7/3/01, have been found persuasive." (Paper No. 7, Office Action mailed March 12, 2002, page 2). Applicants respectfully submit that such arguments should again be found persuasive, and the rejections withdrawn.

#### Rejection Under 35 U.S.C. §112, First Paragraph

Claims 44 and 45 have been rejected as lacking support in the written description for reciting "in pyridine at reflux temperature followed by reflux in the presence of acetic anhydride." Applicants respectfully traverse the rejection for the following reasons.

In issuing a rejection based on a lack of written description, the Examiner bears a burden "of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." as set forth in the MPEP § 2163.04 (emphasis added). To date, this burden has not been taken up by the Examiner.

Applicants respectfully submit that one of ordinary skill in the art, at the time of the filing of the invention, would have been reasonably apprised that applicants were in possession of the invention claimed in pending claims 44-49.

The Examiner has asserted that "the phrase [regarding the reflux steps at issue] is included in a specific example, ... therefore the specification does not support the step [at issue] as being useful in the preparation of ALL compounds of claims 44 and 45. (Office Action, page 6; underlined emphasis added, capitalized emphasis in original). Applicants respectfully submit that no such logical relationship exists.

Viewing the general process description of this conversion (Scheme II, page 11), and example on page 16, lines 5-11 pertinent to this conversion, one of ordinary skill in the art would conclude that each of the compounds of claims 44 and 45 could be prepared in this way, and that this was reasonably conveyed by applicants at the time of filing. That is, compounds within the scope of the pending claims “can also be prepared by condensation of the piperazines of Formula V with the anhydrides of Formula IV.” (page 11, lines 3-5) One of ordinary skill in the art could then look to the examples for further guidance as to the particular teachings of applicants’ specification. One of ordinary skill in the art would understand that this reaction, taking place “in pyridine at reflux temperature followed by reflux in the presence of acetic anhydride” represents general reaction conditions for transformations described in Scheme II.

In fact, the prior art under discussion in this prosecution discloses that these reactions may be carried out using these reagents. For example, Khadilkar et al., in the first paragraph on page 530, discloses preparation of 1-[3-(4-(4-methylphenyl)-1-piperazinyl)propyl]-2,5-pyrrolidinedione, HCl using compound 7d and succinic anhydride, which were “refluxed in dry pyridine....Acetic anhydride... was added and the mixture was further refluxed...” (emphasis added). Similarly, Wu et al., in the last full paragraph in the left column on page 881, discloses preparation of N-[ $\omega$ -(4-phenyl-1-piperazinyl)alkyl]cyclic imides by reflux in dry pyridine, followed by refluxing in acetic acid (i.e., Ac<sub>2</sub>O). Thus, it is clear that one of ordinary skill in the art would have understood that applicants have enabled the claimed method for the entire scope of the claims.

As an aside, Applicants point out that the Office Action misstates the burden to be assumed by the Examiner; that is, it is not the quotation from In re Smith (see Office Action, page 6). rather it is that burden cited above from MPEP §2163.04.

Applicants submit that the claims are supported by the disclosure as filed, and respectfully request reconsideration and withdrawal of the rejection. This would overcome all outstanding rejections and result in allowable claims.

Conclusion

In view of the foregoing, Applicants believe that the present application is now in condition for allowance and respectfully request consideration thereof. A clean copy of claims as amended is submitted herewith, and authorization is hereby given to charge any fees deemed to be due in connection with this Amendment ~~Accompanying Request for Continued Examination~~ to Deposit Account No. 50-0912.

Respectfully submitted,

ANAND *et al.*

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